Amendments to the claims:

This listing of claims replaces all prior versions, and listings, of claims in the application.

Listing of claims:

1 (currently amended): A method of diagnosing or prognostication a neurodegenerative disease in a subject, or determining whether a subject is at increased risk of developing said disease, comprising:

determining a level and/or an activity of

(i) a transcription product of the gene coding for the voltage-gated ion channel sodium channel type 2A (SCN2A)[,] and/or

(ii) a translation product of the gene coding for the voltage-gated ion channel SCN2A ~~and/or~~

~~(iii) a fragment, or derivative, or variant of said transcription or translation product,~~

in a sample from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby diagnosing or prognosticating said neurodegenerative disease in said subject, or determining whether said subject is at increased risk of developing said neurodegenerative disease.

2 (currently amended): A method of monitoring the progression of a neurodegenerative disease in a subject, comprising:

determining a level and/or an activity of

(i) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or

(ii) a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~and/or~~

~~(iii) a fragment, or derivative, or variant of said transcription or translation product,~~

in a sample from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby monitoring the progression of said neurodegenerative disease in said subject.

Claims 3 and 4 (cancelled).

5 (previously presented) The method according to any of claims 1 to 4 wherein said sample comprises a cell, or a tissue, or a body fluid, in particular cerebrospinal fluid or blood.

6 (currently amended) The method according to claim 1 wherein said reference value is that of a level and/or an activity of

(i) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or

(ii) a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~and/or~~

~~(iii) a fragment, or derivative, or variant of said transcription or translation product,~~

in a sample from a subject not suffering from said neurodegenerative disease.

7 (currently amended) The method according to any of claim 1 wherein an alteration in the level and/or activity of a transcription product of the gene coding for the voltage-gated ion channel SCN2A and/or a translation product of the gene coding for voltage-gated ion channel SCN2A ~~and/or a fragment, or derivative, or variant thereof~~, in a sample cell, or tissue, or body fluid, in particular cerebrospinal fluid, from said subject relative to a reference value representing a known health status indicates a diagnosis~~, or prognosis, or increased risk~~ of Alzheimer's disease in said subject.

8 (currently amended) The method according to any of claim 1 , further comprising comparing a level and/or an activity of

(i) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or

(ii) a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~and/or~~

~~(iii) a fragment, or derivative, or variant of said transcription or translation product,~~

in a series of samples taken from said subject over a period of time.

9 (original) The method according to claim 8 wherein said subject receives a treatment prior to one or more of said sample gatherings.

10 (original) The method according to claim 9 wherein said level and/or activity is determined before and after said treatment of said subject.

11 (currently amended): A kit for diagnosing ~~or prognosticating a neurodegenerative disease, in particular~~ Alzheimer's disease[,] in a subject~~, or determining the propensity or predisposition of a subject to develop such a disease,~~ said kit comprising:

(a) at least one reagent which is selected from the group consisting of

(i) reagents that selectively detect a transcription product of the gene coding for the voltage-gated ion channel SCN2A (ii) reagents that selectively detect a translation product of the gene coding for the voltage-gated ion channel SCN2A, and

(b) an instruction for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease~~, or determining the propensity or predisposition of a subject to develop such a disease~~ by

(i) detecting a level, or an activity, or both said level and said activity, of said transcription product and/or said translation product of the gene coding for the voltage-gated ion channel SCN2A in a sample from said subject; and

(ii) diagnosing ~~or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, or determining the propensity or predisposition of said subject to develop such a disease,~~ wherein a varied level, or activity, or both said level and said activity, of said transcription product and/or said translation product compared to a reference value representing a known

health status; or a level, or activity, or both said level and said activity, of said transcription product and/or said translation product similar or equal to a reference value representing a known disease status indicates a diagnosis ~~or prognosis~~ of ~~a neurodegenerative disease, in particular~~ Alzheimer's disease~~, or an increased propensity or predisposition of developing such a disease~~.

12 (currently amended): A method of treating ~~or preventing a neurodegenerative disease, in particular~~ Alzheimer's disease[,] in a subject comprising administering to said subject in a therapeutically or prophylactically effective amount an agent or agents which directly or indirectly affect an activity and/or a level of (i) the gene coding for the voltage-gated ion channel SCN2A, and/or (ii) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or (iii) a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~and/or (iv) a fragment, or derivative, or variant of (i) to (iii)~~.

13 (currently amended): A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of (i) the gene coding for the voltage-gated ion channel SCN2A and/or (ii) a transcription product of the gene coding for the voltage-gated ion channel SCN2A and/or (iii) a translation product of the gene coding for the voltage-gated ion channel SCN2A~~, and/or (iv) a fragment, or derivative, or variant of (i) to (iii)~~.

14 (currently amended): A pharmaceutical composition comprising a modulator according to claim 13 in combination with a pharmaceutically acceptable carrier or diluent.

15 (currently amended): A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of (i) the gene coding for the voltage-gated ion channel SCN2A, and/or (ii) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or (iii) a translation product of the gene coding for the voltage-gated ion channel SCN2A ~~and/or (iv) a fragment, or derivative, or variant of (i) to (iii)~~ for use in a pharmaceutical composition.

16 (currently amended) Use of a modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of (i) the gene coding for the voltage-gated ion channel SCN2A, and/or (ii) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or (iii) a translation product of the gene coding for the voltage-gated ion channel SCN2A~~, and/or (iv) a fragment, or derivative, or variant of (i) to (iii)~~ for a preparation of a medicament for treating ~~or preventing a neurodegenerative disease, in particular~~ Alzheimer's disease.

17 (currently amended): A kit, comprising in one or more containers, a therapeutically ~~or prophylactically~~ effective amount of the pharmaceutical composition of claim 14.

18 (currently amended): A recombinant, non-human animal comprising a non-native gene sequence coding for the voltage-gated ion channel SCN2A ~~or a fragment, or a derivative, or a variant thereof~~, said animal being obtainable by:

(i) providing a gene targeting construct comprising said gene sequence and a selectable marker sequence, and

(ii) introducing said targeting construct into a stem cell of a non-human animal, and

(iii) introducing said non-human animal stem cell into a non-human embryo, and

(iv) transplanting said embryo into a pseudopregnant non-human animal, and

(v) allowing said embryo to develop to term, and

(vi) identifying a genetically altered non-human animal whose genome comprises a modification of said gene sequence in both alleles, and

(vii) breeding the genetically altered non-human animal of step (vi) to obtain a genetically altered non-human animal whose genome comprises a modification of said endogenous gene, wherein said disruption results in said non-human animal exhibiting a predisposition to developing symptoms of ~~a neurodegenerative~~ Alzheimer's disease ~~or related diseases or disorders~~.

19 (currently amended) Use of the recombinant, non-human animal according to claim 18 for screening, testing, and validating compounds, agents, and modulators in the development of diagnostics and therapeutics to treat ~~neurodegenerative diseases, in particular~~ Alzheimer's disease.

20 (currently amended): An assay for screening for a modulator of ~~neurodegenerative diseases, in particular~~ Alzheimer's disease~~, or related diseases or disorders~~ of one or more substances selected from the group consisting of

(i) the gene coding for the voltage-gated ion channel SCN2A, and/or

(ii) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or

(iii) a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~and/or~~

~~(iv) a fragment, or derivative, or variant of (i) to (iii),~~

said method comprising:

(a) contacting a cell with a test compound;

(b) measuring the activity and/or level of one or more substances recited in (i) to (iv);

(c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a control cell not contacted with said test compound; and

(d) comparing the levels and/or activities of the substance in the cells of step (b) and (c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of said diseases or disorders.

21 (currently amended): A method of screening for a modulator of ~~neurodegenerative diseases, in particular~~ Alzheimer's disease~~, or related diseases or disorders~~ of one or more substances selected from the group consisting of

(i) the gene coding for the voltage-gated ion channel SCN2A, and/or

(ii) a transcription product of the gene coding for the voltage-gated ion channel SCN2A, and/or

(iii) a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~and/or~~

~~(i) a fragment, or derivative, or variant of (i) to (iii),~~

said method comprising:

(a) administering a test compound to a test animal which is predisposed to developing or has already developed symptoms of ~~a neurodegenerative disease or related diseases or disorders in respect of the substances~~ Alzheimer's disease recited in (i) to ~~(iv)~~ (iii);

(b) measuring the activity and/or level of one or more substances recited in ~~(iv)~~ (iii);

(c) measuring the activity and/or level of one or more substances recited in (i) ~~or (iv)~~ in a matched control animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect to the substances recited in (i) to ~~(iv)~~ (iii) and to which animal no such test compound has been administered;

(d) comparing the activity and/or level of the substance in the animals of step (b) and (c), wherein an alteration in the activity and/or level of substances in the test animal

indicates that the test compound is a modulator of ~~said diseases or disorders~~ Alzheimer's disease.

22 (currently amended) The method according to claim 21 wherein said test animal and/or said control animal is a recombinant animal which expresses the voltage-gated ion channel SCN2A, ~~or a fragment, or a derivative, or a variant thereof,~~ under the control of a transcriptional control element which is not the native SCN2A gene transcriptional control element.

23 (currently amended): A method of testing a compound, preferably of screening a plurality of compounds, for inhibition of binding between a ligand and the voltage-gated ion channel SCN2A, ~~or a fragment, or derivative, or variant thereof,~~ said method comprising the steps of:

(i) adding a liquid suspension of said voltage-gated ion channel SCN2A, ~~or a fragment, or derivative, or variant thereof,~~ to a plurality of containers;

(ii) adding a compound, preferably a plurality of compounds, to be screened for said inhibition of binding to said plurality of containers;

(iii) adding a detectable ligand, in particular a fluorescently detectable ligand, to said containers;

(iv) incubating the liquid suspension of said voltage-gated ion channel SCN2A, ~~or said fragment, or derivative, or variant thereof,~~ and said compound, preferably said plurality of compounds, and said ligand;

(v) measuring amounts of detectable ligand or fluorescence associated with said voltage-gated ion channel SCN2A~~, or with said fragment, or derivative, or variant thereof~~; and

(vi) determining the degree of inhibition by one or more of said compounds of binding of said ligand to said voltage-gated ion channel SCN2A, or said fragment~~, or derivative, or variant thereof~~.

24 (currently amended): A method of testing a compound, preferably of screening a plurality of compounds, to determine the degree of binding of said compound or compounds to the voltage-gated ion channel SCN2A, ~~or to a fragment, or derivative, or variant thereof,~~ said method comprising the steps of:

(i) adding a liquid suspension of said voltage-gated ion channel SCN2A, ~~or a fragment, or derivative, or variant thereof,~~ to a plurality of containers;

(ii) adding a detectable compound, preferably a plurality of detectable compounds, in particular fluorescently detectable compounds, to be screened for said binding to said plurality of containers;

(iii) incubating the liquid suspension of said voltage-gated ion channel SCN2A,~~ or said fragment, or derivative, or variant thereof,~~ and said compound, preferably said plurality of compounds;

(iv) measuring amounts of detectable compound or fluorescence associated with said voltage-gated ion channel SCN2A~~, or with said fragment, or derivative, or variant thereof~~, and

(v) determining the degree of binding by one or more of said compounds to said voltage-gated ion channel SCN2A~~, or said fragment, or derivative, or variant thereof~~.

25 (previously presented): A method for producing a medicament comprising the steps of (i) identifying a modulator of ~~neurodegenerative diseases, in particular~~ Alzheimer's disease[,] by a method according to claim 20 and (ii) admixing the modulator with a pharmaceutical carrier.

26 (original): A method for producing a medicament comprising the steps of (i) identifying a compound as an inhibitor of binding between a ligand and the SCN2A gene product by a method according to claim 23 and (ii) admixing the compound with a pharmaceutical carrier.

27 (original): A method for producing a medicament comprising the steps of (i) identifying a compound as a binder to a SCN2A gene product by a method according to claim 24 and (ii) admixing the compound with a pharmaceutical carrier.

28 (previously presented): A medicament obtainable by the method according to claim 25.

29 (previously presented): A medicament obtained by the method according to claim 25.

30 (currently amended) A protein molecule, said protein molecule being a translation product of the gene coding for the voltage-gated ion channel SCN2A, ~~or a fragment, or derivative, or variant thereof,~~ for use as a diagnostic target for detecting ~~a neurodegenerative disease, preferably~~ Alzheimer's disease.

31 (currently amended): A protein molecule, said protein molecule being a translation product of the gene coding for the voltage-gated ion channel SCN2A, or a fragment, ~~or derivative, or variant thereof,~~ for use as a screening target for reagents or compounds preventing~~, or treating, or ameliorating a neurodegenerative disease, preferably~~ Alzheimer's disease.

32 (currently amended) Use of an antibody specifically immunoreactive with an immunogen, wherein said immunogen is a translation product of the gene coding for the voltage-gated ion channel SCN2A~~, or a fragment, or derivative, or variant thereof,~~ for detecting the pathological state of a cell in a sample from a subject, comprising immunocytochemical staining of said cell with said antibody, wherein an altered degree of staining, or an altered staining pattern in said cell compared to a cell representing a known health status indicates a pathological state of said cell.